Roles of heat shock factor 1 in neuronal response to fetal environmental risks and its relevance to brain disorders.

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Public Summary:
Although prenatal exposure to such environmental factors as alcohol, methylmercury and maternal seizure can contribute to adult-onset neuropsychiatric disorders, the mechanism by which these exposures impact brain development remains unclear. Exposure of mouse embryos to these environmental factors led to increased expression of the stress response gene HSF-1 in the brain. Furthermore, in mice lacking normal HSF-1 levels, these environmental stimuli led to exaggerated effects, including aberrant on brain morphology and increased seizures. Finally, in human brain cells derived from patients with schizophrenia, we also observed altered changes in HSF-1 levels in response to these environmental stimuli. HSF-1 response may be a key mediator by which these fetal exposures lead to later brain disorders.

Scientific Abstract:
Prenatal exposure of the developing brain to various environmental challenges increases susceptibility to late onset of neuropsychiatric dysfunction; still, the underlying mechanisms remain obscure. Here we show that exposure of embryos to a variety of environmental factors such as alcohol, methylmercury, and maternal seizure activates HSF1 in cerebral cortical cells. Furthermore, Hsf1 deficiency in the mouse cortex exposed in utero to subthreshold levels of these challenges causes structural abnormalities and increases seizure susceptibility after birth. In addition, we found that human neural progenitor cells differentiated from induced pluripotent stem cells derived from schizophrenia patients show higher variability in the levels of HSF1 activation induced by environmental challenges compared to controls. We propose that HSF1 plays a crucial role in the response of brain cells to prenatal environmental insults and may be a key component in the pathogenesis of late-onset neuropsychiatric disorders.